

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior listings of claims presented in the application.

Claims 1-12 (Canceled)

Claim 13 (Currently Amended): A method ~~for~~ of subcutaneously administering a biologically active agent, said method comprising:

- (a) providing a biologically active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to said native state and is conformationally between said native and denatured states; and
- (b) exposing said biologically active agent to a complexing perturbant to reversibly transform said biologically active agent to said intermediate state and to form a subcutaneously deliverable supramolecular complex, and
- (c) administering subcutaneously ~~administering~~ said supramolecular complex said perturbant having a molecular weight ranging from about 150 to about 600 daltons, and having at least one hydrophilic moiety and at least one hydrophobic moiety, said supramolecular complex comprising said perturbant non-covalently complexed with said biologically active agent; and said biologically active agent not forming a microsphere with said perturbant; wherein said perturbant is in an amount effective for subcutaneous delivery of said biologically active agent;

wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

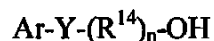
R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

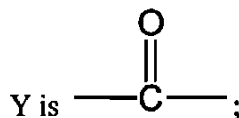
a salt thereof, and

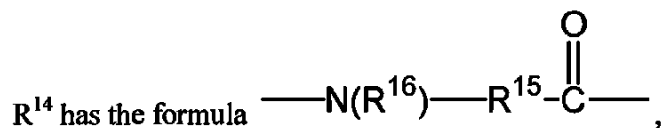
(b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;





R^{15} is C_1 to C_{24} alkyl, C_2 to C_{24} alkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl) phenyl, (C_2 to C_{10} alkenyl) phenyl, (C_1 to C_{10} alkyl) naphthyl, (C_2 to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_2 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl), and naphthyl (C_2 to C_{10} alkenyl);

R^{15} is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH, -CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R^{17} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;


R^{15} is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R^{16} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

and n is from 1 to 5, or salt thereof.

Claim 14 (Original): A method as defined in claim 13, wherein said intermediate state has ΔG ranging from about -20 kcal/mole to about 20 kcal/moles relative to said native state.

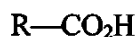
Claim 15 (Original): A method as defined in claim 13, wherein said biologically active agent is selected from the group consisting of a peptide, a micropolysaccharide, a carbohydrate, a lipid, a pesticide, or any combination of the foregoing.

Claim 16 (Previously Presented): A method as defined in claim 15, wherein said biologically-active agent is selected from the group consisting of human growth hormone, bovine {W:\01946\100a483-us8\01011776.DOC  }

growth hormone, growth hormone-releasing hormone, an interferon, interleukin-II, insulin, heparin, calcitonin, erythropoietin, atrial naturetic factor, an antigen, a monoclonal antibody, somatostatin, adrenocorticotropin, gonadotropin releasing hormone, oxytocin, vasopressin, cromolyn sodium, vancomycin, desferrioxamine (DFO), low molecular weight heparin, antimicrobials, or any combination of any of the foregoing.

Claims 17 -21 (Canceled)

Claim 22 (Previously Presented): A method as defined in claim 13, wherein said perturbant comprises a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

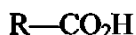
a salt thereof.

Claim 23 (Currently Amended): A method ~~for~~ of subcutaneously administering a biologically active agent comprising:

(a) providing a biologically active agent in an intermediate conformational state non-covalently complexed with a complexing perturbant having a molecular weight ranging from about 150 to about 600 and having at least one hydrophilic moiety and at least one hydrophobic moiety; and

(b) administering subcutaneously ~~administering~~ said biologically active agent wherein said intermediate state is reversible to said native state and is conformationally between a native conformational and a denatured conformational state of said biologically active agent and said composition is not a microsphere; and wherein said perturbant is in an amount effective for subcutaneous delivery of said biologically active agent;

wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

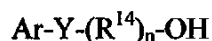
R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

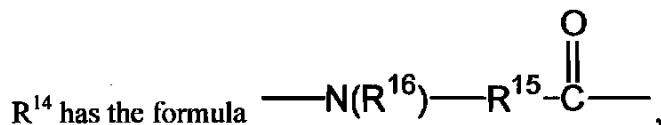
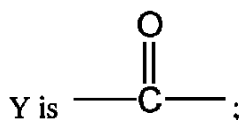
a salt thereof, and

(b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R¹⁵ is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl) phenyl, (C₂ to C₁₀ alkenyl) phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl) naphthyl, phenyl (C₁ to C₁₀ alkyl), phenyl (C₂ to C₁₀ alkenyl), naphthyl (C₁ to C₁₀ alkyl), and naphthyl (C₂ to C₁₀ alkenyl);

R¹⁵ is optionally substituted with C₁ to C₄ alkyl, C₁ to C₄ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R¹⁷ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

R¹⁵ is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R¹⁶ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

and n is from 1 to 5, or salt thereof.

Claim 24 (Previously Presented): A method as defined in claim 23, wherein said biologically active agent is selected from the group consisting of a peptide, a micropolysaccharide, a carbohydrate, a lipid, a pesticide, or any combination of the foregoing.

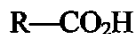
Claim 25 (Previously Presented): A method as defined in claim 24, wherein said biologically-active agent is selected from the group consisting of human growth hormone, bovine growth hormone, growth hormone-releasing hormone, an interferon, interleukin-II, insulin, heparin, calcitonin, erythropoietin, atrial naturetic factor, an antigen, a monoclonal antibody, somatostatin, adrenocorticotropin, gonadotropin releasing hormone, oxytocin, vasopressin, cromolyn sodium, vancomycin, desferrioxamine (DFO), low molecular weight heparin, antimicrobials, or any combination of any of the foregoing.

Claim 26 (Previously Presented): A method as defined in claim 23, wherein said perturbant comprises a proteinoid.

Claims 27 - 30 (Canceled)

Claim 31 (Previously Presented): A method as defined in claim 23, wherein said perturbant comprises a carboxylic acid having the formula

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wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl)naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

a salt thereof.

Claim 32 (Previously Presented): The method of claim 23, wherein said biologically active agent is introduced to

- (a) an excipient,
- (b) a diluent,
- (c) a disintegrant,
- (d) a lubricant,
- (e) a plasticizer,
- (f) a colorant,
- (g) a dosing vehicle, or
- (h) any combination thereof.

Claim 33 (Currently Amended): A method ~~for~~ of subcutaneously administering an active agent said method comprising:

(a) providing a biologically active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to said native state and is conformationally between said native and denatured states;

(b) exposing said biologically active agent to a complexing perturbant to reversibly transform said biologically active agent to said intermediate state and to form a subcutaneously administrable supramolecular complex,

said perturbant having a molecular weight between about 150 and about 600 daltons, and having at least one hydrophilic moiety and one hydrophilic moiety,

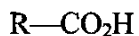
said supramolecular complex comprising said perturbant non-covalently complexed with said biologically active agent, and

said biologically active agent not forming a microsphere with said perturbant;

wherein said perturbant is in an amount effective for subcutaneous delivery of said biologically active agent; and

(c) preparing a mimetic of said supramolecular complex, and

(d) administering subcutaneously ~~administering~~ said mimetic, wherein said perturbant is selected is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂

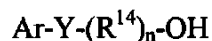
to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

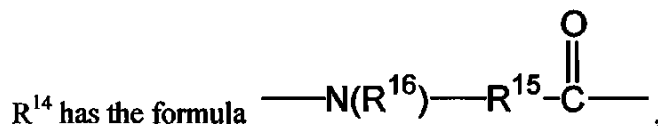
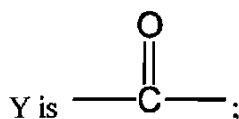
R^1 is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl; or
a salt thereof, and

(b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R¹⁵ is C₁ to C₂₄ alkyl, C₂to C₂₄ alkenyl, phenyl, naphthyl, (C₁to C₁₀ alkyl) phenyl, (C₂to C₁₀ alkenyl) phenyl, (C₁to C₁₀ alkyl) naphthyl, (C₂to C₁₀ alkenyl) naphthyl, phenyl (C₁to C₁₀ alkyl), phenyl (C₂to C₁₀ alkenyl), naphthyl (C₁to C₁₀ alkyl), and naphthyl (C₂to C₁₀ alkenyl);

R¹⁵ is optionally substituted with C₁ to C₄ alkyl, C₁ to C₄ alkenyl, C₁ to C₄ alkoxy, -OH, -SH,

-CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R¹⁷ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

R¹⁵ is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

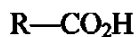
R¹⁶ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

and n is from 1 to 5, or salt thereof.

Claim 34 (Original): A method as defined in claim 33, wherein said biologically active agent comprises a peptide and said mimetic comprises a peptide mimetic.

Claim 35 (Currently Amended): A method ~~for~~ of subcutaneously administering a biologically active agent, said method comprising:

- (a) providing a biologically active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate which is reversible to said native state and is conformationally between said native and denatured states;
- (b) exposing said biologically active agent to a perturbant to reversibly transform said biologically active agent to said intermediate state, wherein said perturbant is in an amount effective for subcutaneous delivery of said biologically active agent; and
- (c) preparing a mimetic of said intermediate state, and
- (d) administering subcutaneously ~~administering~~ said mimetic, wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

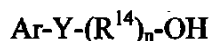
R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

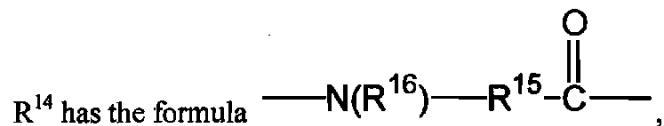
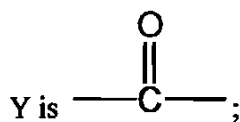
a salt thereof, and

(b) an acylated amino acid having the formula having the formula:




wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R¹⁵ is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl) phenyl, (C₂ to C₁₀ alkenyl) phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl) naphthyl, phenyl (C₁ to C₁₀ alkyl),

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phenyl (C₂ to C₁₀ alkenyl), naphthyl (C₁ to C₁₀ alkyl), and naphthyl (C₂ to C₁₀ alkenyl);

R¹⁵ is optionally substituted with C₁ to C₄ alkyl, C₁ to C₄ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R¹⁷ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

R¹⁵ is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R¹⁶ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

and n is from 1 to 5, or salt thereof.

Claim 36 (Previously Presented): A method as defined in claim 35, wherein said perturbant further comprises a pH changing agent, an ionic strength changing agent, or guanidine hydrochloride.

Claims 37-49 (Canceled)

Claim 50 (Currently Amended): A method ~~for~~ of sublingually administering a biologically active agent, said method comprising:

- (a) providing a biologically active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to said native state and is conformationally between said native and denatured states; and
- (b) exposing said biologically active agent to a complexing perturbant to reversibly transform said biologically active agent to said intermediate state and to form a sublingually

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administrable supramolecular complex, and

(c) administering sublingually ~~administering~~ said supramolecular complex

said perturbant having a molecular weight ranging from about 150 to about 600 daltons, and having at least one hydrophilic moiety and at least one hydrophobic moiety,

said supramolecular complex comprising said perturbant non-covalently complexed with said biologically active agent; and

said biologically active agent not forming a microsphere with said perturbant;

wherein said perturbant is in an amount effective for sublingual delivery of said biologically active agent;

wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



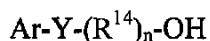
wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

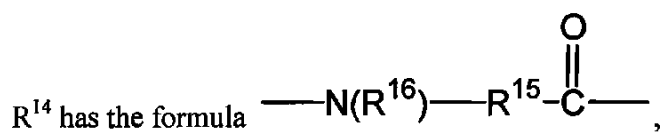
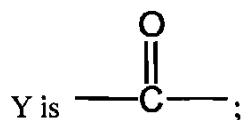
R^1 is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl; or
a salt thereof, and

(b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R^{15} is C_1 to C_{24} alkyl, C_2 to C_{24} alkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl) phenyl, (C_2 to C_{10} alkenyl) phenyl, (C_1 to C_{10} alkyl) naphthyl, (C_2 to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_2 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl), and naphthyl (C_2 to C_{10} alkenyl);

R^{15} is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH, $\text{-CO}_2\text{R}^{17}$, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R^{17} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

R^{15} is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R^{16} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

and n is from 1 to 5, or salt thereof.

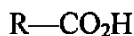
Claim 51 (Original): A method as defined in claim 50, wherein said intermediate state has ΔG ranging from about -20 kcal/mole to about 20 kcal/moles relative to said native state.

Claim 52 (Original): A method as defined in claim 50, wherein said biologically active agent is selected from the group consisting of a peptide, a micropolysaccharide, a carbohydrate, a lipid, a pesticide, or any combination of the foregoing.


Claim 53 (Previously Presented): A method as defined in claim 52, wherein said biologically-active agent is selected from the group consisting of human growth hormone, bovine growth hormone, growth hormone-releasing hormone, an interferon, interleukin-II, insulin, heparin, calcitonin, erythropoietin, atrial naturetic factor, an antigen, a monoclonal antibody, somatostatin, adrenocorticotropin, gonadotropin releasing hormone, oxytocin, vasopressin, cromolyn sodium, vancomycin, desferrioxamine (DFO), low molecular weight heparin, antimicrobials, or any combination of any of the foregoing.

Claims 54 -58 (Canceled).

Claim 59 (Previously Presented): A method as defined in claim 50, wherein said perturbant comprises a carboxylic acid having the formula



wherein R is C_1 to C_{24} alkyl, C_2 to C_{24} alkenyl, C_3 to C_{10} cycloalkyl, C_3 to C_{10} cycloalkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl)phenyl, (C_2 to C_{10} alkenyl)phenyl, (C_1 to C_{10} alkyl)naphthyl, (C_2

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to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

a salt thereof.

Claim 60 (Currently Amended): A method ~~for~~ of sublingually administering a biologically active agent comprising:

(a) providing a biologically active agent in an intermediate conformational state non-covalently complexed with a complexing perturbant having a molecular weight ranging from about 150 to about 600 and having at least one hydrophilic moiety and at least one hydrophobic moiety;

(b) administering sublingually ~~administering~~ said biologically active agent

wherein said intermediate state is reversible to said native state and is conformationally between a native conformational and a denatured conformational state of said biologically active agent and said composition is not a microsphere; and wherein said perturbant is in an amount effective for sublingual delivery of said biologically active agent;

wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula :



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

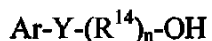
R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

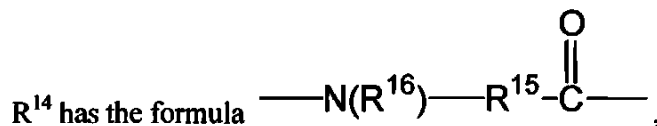
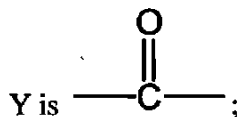
a salt thereof, and

(b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R¹⁵ is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl) phenyl, (C₂ to C₁₀

alkenyl) phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl) naphthyl, phenyl (C₁ to C₁₀ alkyl), phenyl (C₂ to C₁₀ alkenyl), naphthyl (C₁ to C₁₀ alkyl), and naphthyl (C₂ to C₁₀ alkenyl);

R¹⁵ is optionally substituted with C₁ to C₄ alkyl, C₁ to C₄ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R¹⁷ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

R¹⁵ is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R¹⁶ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

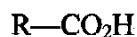
and n is from 1 to 5, or salt thereof.

Claim 61 (Previously Presented): A method as defined in claim 60, wherein said biologically active agent is selected from the group consisting of a peptide, a micropolysaccharide, a carbohydrate, a lipid, a pesticide, or any combination of the foregoing.

Claim 62 (Previously Presented): A method as defined in claim 61, wherein said biologically-active agent is selected from the group consisting of human growth hormone, bovine growth hormone, growth hormone-releasing hormone, an interferon, interleukin-II, insulin, heparin, calcitonin, erythropoietin, atrial naturetic factor, an antigen, a monoclonal antibody, somatostatin, adrenocorticotropin, gonadotropin releasing hormone, oxytocin, vasopressin, cromolyn sodium, vancomycin, desferrioxamine (DFO), low molecular weight heparin, anitmicrobials, or any combination of any of the foregoing.

Claims 63 - 67 (Canceled).

Claim 68 (Previously Presented): A method as defined in claim 60, wherein said perturbant comprises a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl)naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

a salt thereof.

Claim 69 (Previously Presented): A method as defined in claim 60, wherein said biologically active agent is introduced to:

- (a) an excipient,
- (b) a diluent,
- (c) a disintegrant,
- (d) a lubricant,

- (e) a plasticizer,
- (f) a colorant,
- (g) a dosing vehicle, or
- (h) any combination thereof.

Claim 70 (Currently Amended): A method ~~for~~ of sublingually administering an agent to a subject in need of said agent, said method comprising:

(a) providing a biologically active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to said native state and is conformationally between said native and denatured states;

(b) exposing said biologically active agent to a complexing perturbant to reversibly transform said biologically active agent to said intermediate state and to form a sublingually administrable supramolecular complex,

said perturbant having a molecular weight between about 150 and about 600 daltons, and having at least one hydrophilic moiety and one hydrophilic moiety,

said supramolecular complex comprising said perturbant non-covalently complexed with said biologically active agent, and

said biologically active agent not forming a microsphere with said perturbant;

wherein said perturbant is in an amount effective for sublingual delivery of said biologically active agent; and

(c) preparing a mimetic of said supramolecular complex, and

(d) administering sublingually ~~administering~~ said mimetic, wherein said perturbant is

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selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

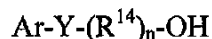
R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

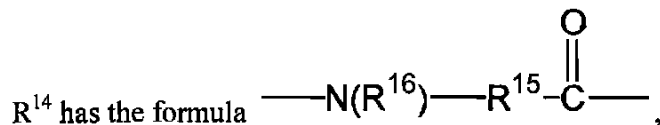
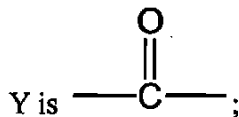
a salt thereof, and

(b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R¹⁵ is C₁ to C₂₄ alkyl, C₂to C₂₄ alkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl) phenyl, (C₂ to C₁₀ alkenyl) phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl) naphthyl, phenyl (C₁ to C₁₀ alkyl), phenyl (C₂ to C₁₀ alkenyl), naphthyl (C₁ to C₁₀ alkyl), and naphthyl (C₂ to C₁₀ alkenyl);

R¹⁵ is optionally substituted with C₁ to C₄ alkyl, C₁ to C₄ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R¹⁷ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

R¹⁵ is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R¹⁶ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl;

and n is from 1 to 5, or salt thereof.

Claim 71 (Original): A method as defined in claim 70, wherein said biologically active agent comprises a peptide and said mimetic comprises a peptide mimetic.

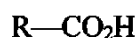
Claim 72 (Currently Amended): A method ~~for~~ of sublingually administering a biologically active agent to a subject in need of said agent, said method comprising:

(a) providing a biologically active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate which is reversible to said native state and is conformationally between said native and denatured states;

(b) exposing said biologically active agent to a perturbant to reversibly transform said biologically active agent to said intermediate state, wherein said perturbant is in an amount effective for sublingual delivery of said biologically active agent; and

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- (c) preparing a mimetic of said intermediate state, and
- (d) administering sublingually ~~administering~~ said mimetic, wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

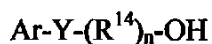
R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

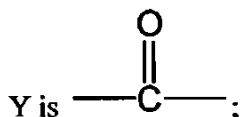
a salt thereof, and

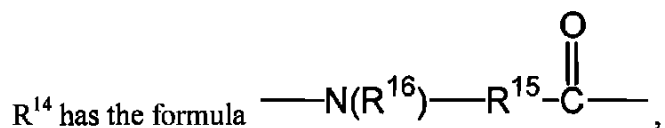
- (b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;





R^{15} is C_1 to C_{24} alkyl, C_2 to C_{24} alkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl) phenyl, (C_2 to C_{10} alkenyl) phenyl, (C_1 to C_{10} alkyl) naphthyl, (C_2 to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_2 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl), and naphthyl (C_2 to C_{10} alkenyl);

R^{15} is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH, -CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R^{17} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

R^{15} is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R^{16} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;


and n is from 1 to 5, or salt thereof.

Claim 73 (Original): A method as defined in claim 72, wherein said perturbant further comprises a pH changing agent, an ionic strength changing agent, or guanidine hydrochloride.

Claims 74-86 (Canceled)

Claim 87 (Currently Amended): A method for of intranasally administering a biologically active agent, said method comprising:

(a) providing a biologically active agent which can exist in a native conformational state,

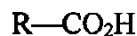
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a denatured conformational state, and an intermediate conformational state which is reversible to said native state and is conformationally between said native and denatured states; and

(b) exposing said biologically active agent to a complexing perturbant to reversibly transform said biologically active agent to said intermediate state and to form an intranasally administrable supramolecular complex, and

(c) administering intranasally ~~administering~~ said supramolecular complex, said perturbant having a molecular weight ranging from about 150 to about 600 daltons, and having at least one hydrophilic moiety and at least one hydrophobic moiety, said supramolecular complex comprising said perturbant non-covalently complexed with said biologically active agent; and said biologically active agent not forming a microsphere with said perturbant; wherein said perturbant is in an amount effective for intranasal delivery of said biologically active agent;

wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH,

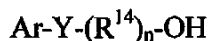
-SH, $-\text{CO}_2\text{R}^1$, C_3 to C_{10} cycloalkyl, C_3 to C_{10} cycloalkenyl, aryl, $(\text{C}_1$ to C_{10} alkyl)aryl, aryl(C_1 to C_{10})alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R^1 is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl; or

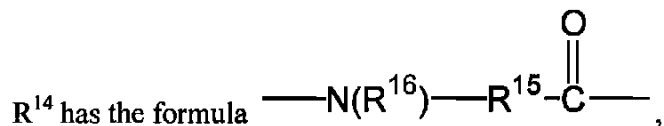
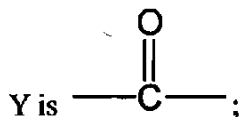
a salt thereof, and

(b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R^{15} is C_1 to C_{24} alkyl, C_2 to C_{24} alkenyl, phenyl, naphthyl, $(\text{C}_1$ to C_{10} alkyl) phenyl, $(\text{C}_2$ to C_{10} alkenyl) phenyl, $(\text{C}_1$ to C_{10} alkyl) naphthyl, $(\text{C}_2$ to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_2 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl), and naphthyl (C_2 to C_{10} alkenyl);

R^{15} is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH, $-\text{CO}_2\text{R}^{17}$, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R^{17} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

R^{15} is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and
 R^{16} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;
and n is from 1 to 5, or salt thereof.

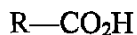
Claim 88 (Original): A method as defined in claim 87, wherein said intermediate state has ΔG ranging from about -20 kcal/mole to about 20 kcal/moles relative to said native state.

Claim 89 (Original): A method as defined in claim 87, wherein said biologically active agent is selected from the group consisting of a peptide, a micropolysaccharide, a carbohydrate, a lipid, a pesticide, or any combination of the foregoing.

Claim 90 (Previously Presented): A method as defined in claim 89, wherein said biologically-active agent is selected from the group consisting of human growth hormone, bovine growth hormone, growth hormone-releasing hormone, an interferon, interleukin-II, insulin, heparin, calcitonin, erythropoietin, atrial naturetic factor, an antigen, a monoclonal antibody, somatostatin, adrenocorticotropin, gonadotropin releasing hormone, oxytocin, vasopressin, cromolyn sodium, vancomycin, desferrioxamine (DFO), low molecular weight heparin, antimicrobials, or any combination of any of the foregoing.

Claims 91-95 (Canceled).

Claim 96 (Previously Presented): A method as defined in claim 87, wherein said perturbant comprises a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl)naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

a salt thereof.

Claim 97 (Currently Amended): A method ~~for~~ of intranasally administering a biologically active agent comprising:

(a) providing a biologically active agent in an intermediate conformational state non-covalently complexed with a complexing perturbant having a molecular weight ranging from about 150 to about 600 and having at least one hydrophilic moiety and at least one hydrophobic moiety; and

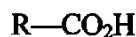
(b) ~~administering intranasally administering~~ said biologically active agent

wherein said intermediate state is reversible to said native state and is conformationally

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between a native conformational and a denatured conformational state of said biologically active agent and said composition is not a microsphere; and wherein said perturbant is in an amount effective for intranasal delivery of said biologically active agent;

wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

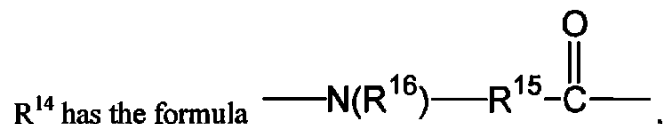
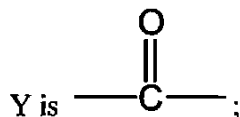
a salt thereof, and

(b) an acylated amino acid having the formula having the formula:



wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R^{15} is C_1 to C_{24} alkyl, C_2 to C_{24} alkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl) phenyl, (C_2 to C_{10} alkenyl) phenyl, (C_1 to C_{10} alkyl) naphthyl, (C_2 to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_2 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl), and naphthyl (C_2 to C_{10} alkenyl);

R^{15} is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH, -CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R^{17} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

R^{15} is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R^{16} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

and n is from 1 to 5, or salt thereof.

Claim 98 (Previously Presented): A method as defined in claim 97, wherein said biologically active agent is selected from the group consisting of a peptide, a micropolysaccharide, a carbohydrate, a lipid, a pesticide, or any combination of the foregoing.

Claim 99 (Previously Presented): A method as defined in claim 98, wherein said biologically-active agent is selected from the group consisting of human growth hormone, bovine

growth hormone, growth hormone-releasing hormone, an interferon, interleukin-II, insulin, heparin, calcitonin, erythropoietin, atrial natriuretic factor, an antigen, a monoclonal antibody, somatostatin, adrenocorticotropin, gonadotropin releasing hormone, oxytocin, vasopressin, cromolyn sodium, vancomycin, desferrioxamine (DFO), low molecular weight heparin, antimicrobials, or any combination of any of the foregoing.

Claims 100 - 104 (Canceled).

Claim 105 (Previously Presented): A method as defined in claim 97, wherein said perturbant comprises a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl)naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

a salt thereof.

Claim 106 (Currently Amended): A method as defined in claim 97 93, wherein said biologically active is introduced to:

- (a) an excipient,
- (b) a diluent,
- (c) a disintegrant,
- (d) a lubricant,
- (e) a plasticizer,
- (f) a colorant,
- (g) a dosing vehicle, or
- (h) any combination thereof.

Claim 107 (Currently Amended): A method ~~for~~ of intranasally administering a biologically active agent to a subject in need of said agent, said method comprising:

(a) providing a biologically active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to said native state and is conformationally between said native and denatured states;

(b) exposing said biologically active agent to a complexing perturbant to reversibly transform said biologically active agent to said intermediate state and to form an intranasally administrable supramolecular complex,

said perturbant having a molecular weight between about 150 and about 600 daltons, and having at least one hydrophilic moiety and one hydrophilic moiety,

said supramolecular complex comprising said perturbant non-covalently complexed

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with said biologically active agent, and

said biologically active agent not forming a microsphere with said perturbant;

wherein said perturbant is in an amount effective for intranasal delivery of said biologically active agent; and

(c) preparing a mimetic of said supramolecular complex, and

(d) administering intranasally ~~administering~~ said supramolecular complex, wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

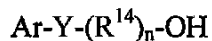
R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;

R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and


R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

a salt thereof, and

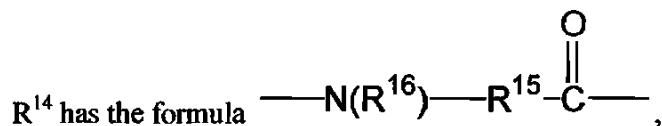
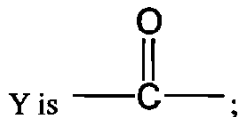
(b) an acylated amino acid having the formula having the formula:



wherein:

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Ar is a substituted or unsubstituted phenyl or naphthyl;



R^{15} is C_1 to C_{24} alkyl, C_2 to C_{24} alkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl) phenyl, (C_2 to C_{10} alkenyl) phenyl, (C_1 to C_{10} alkyl) naphthyl, (C_2 to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_2 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl), and naphthyl (C_2 to C_{10} alkenyl);

R^{15} is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH, -CO₂R¹⁷, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R^{17} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

R^{15} is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R^{16} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

and n is from 1 to 5, or salt thereof.

Claim 108 (Original): A method as defined in claim 107, wherein said biologically active agent comprises a peptide and said mimetic comprises a peptide mimetic.

Claim 109 (Currently Amended): A method ~~for~~ of intranasally administering a biologically active agent to a subject in need of said agent, said method comprising:

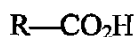
(a) providing a biologically active agent which can exist in a native conformational state,

a denatured conformational state, and an intermediate which is reversible to said native state and is conformationally between said native and denatured states;

(b) exposing said biologically active agent to a perturbant to reversibly transform said biologically active agent to said intermediate state, wherein said perturbant is in an amount effective for intranasal delivery of said biologically active agent; and

(c) preparing a mimetic of said intermediate state, and

(d) administering intranasally ~~administering~~ said biologically active agent, wherein said perturbant is selected from the group consisting of (a) a carboxylic acid having the formula



wherein R is C₁ to C₂₄ alkyl, C₂ to C₂₄ alkenyl, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, phenyl, naphthyl, (C₁ to C₁₀ alkyl)phenyl, (C₂ to C₁₀ alkenyl)phenyl, (C₁ to C₁₀ alkyl) naphthyl, (C₂ to C₁₀ alkenyl)naphthyl, phenyl(C₁ to C₁₀ alkyl), phenyl(C₂ to C₁₀ alkenyl), naphthyl(C₁ to C₁₀ alkyl) and naphthyl(C₂ to C₁₀ alkenyl);

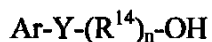
R being optionally substituted with C₁ to C₁₀ alkyl, C₂ to C₁₀ alkenyl, C₁ to C₄ alkoxy, -OH, -SH, -CO₂R¹, C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ cycloalkenyl, aryl, (C₁ to C₁₀ alkyl)aryl, aryl(C₁ to C₁₀)alkyl, or any combination thereof;


R being optionally interrupted by oxygen, nitrogen, sulfur, or any combination thereof; and

R¹ is hydrogen, C₁ to C₄ alkyl or C₂ to C₄ alkenyl; or

a salt thereof, and

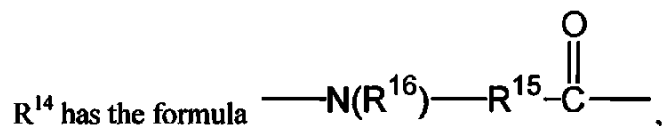
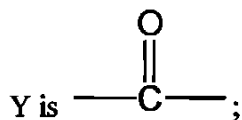
(b) an acylated amino acid having the formula having the formula:



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wherein:

Ar is a substituted or unsubstituted phenyl or naphthyl;



R^{15} is C_1 to C_{24} alkyl, C_2 to C_{24} alkenyl, phenyl, naphthyl, (C_1 to C_{10} alkyl) phenyl, (C_2 to C_{10} alkenyl) phenyl, (C_1 to C_{10} alkyl) naphthyl, (C_2 to C_{10} alkenyl) naphthyl, phenyl (C_1 to C_{10} alkyl), phenyl (C_2 to C_{10} alkenyl), naphthyl (C_1 to C_{10} alkyl), and naphthyl (C_2 to C_{10} alkenyl);

R^{15} is optionally substituted with C_1 to C_4 alkyl, C_1 to C_4 alkenyl, C_1 to C_4 alkoxy, -OH, -SH, $-\text{CO}_2\text{R}^{17}$, cycloalkyl, cycloalkenyl, heterocyclic alkyl, alkaryl, heteroaryl, heteroalkaryl, or any combination thereof;

R^{17} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

R^{15} is optionally interrupted by oxygen, nitrogen, sulfur or any combination thereof; and

R^{16} is hydrogen, C_1 to C_4 alkyl or C_2 to C_4 alkenyl;

and n is from 1 to 5, or salt thereof.

Claim 110 (Previously Presented): A method as defined in claim 109, wherein said perturbant further comprises a pH changing agent, an ionic strength changing agent, or guanidine hydrochloride.

Claim 111 (Canceled).

Claim 112 (Previously Presented): The method of claim 190, wherein the biologically active agent is human growth hormone.

Claim 113 (Previously Presented): The method of claim 190, wherein the biologically active agent is growth-hormone releasing hormone.

Claim 114 (Previously Presented): The method of claim 190, wherein the biologically active agent is insulin.

Claim 115 (Previously Presented): The method of claim 190, wherein the biologically active agent is heparin.

Claim 116 (Previously Presented): The method of claim 190, wherein the biologically active agent is low molecular weight heparin.

Claim 117 (Previously Presented): The method of claim 190, wherein the biologically active agent is calcitonin.

Claim 118 (Previously Presented): The method of claim 190, wherein the biologically active agent is cromolyn sodium.

Claim 119 (Previously Presented): The method of claim 190, wherein the biologically active agent is an antimicrobial.

Claim 120 (Previously Presented): The method of claim 191, wherein the biologically active agent is human growth hormone.

Claim 121 (Previously Presented): The method of claim 191, wherein the biologically active agent is growth-hormone releasing hormone.

Claim 122 (Previously Presented): The method of claim 191, wherein the biologically active agent is insulin.

Claim 123 (Previously Presented): The method of claim 191, wherein the biologically active agent is heparin.

Claim 124 (Previously Presented): The method of claim 191, wherein the biologically active agent is low molecular weight heparin.

Claim 125 (Previously Presented): The method of claim 191, wherein the biologically active agent is calcitonin.

Claim 126 (Previously Presented): The method of claim 191, wherein the biologically active agent is cromolyn sodium.

Claim 127 (Previously Presented): The method of claim 191, wherein the biologically active agent is an antimicrobial.

Claims 128-130 (Canceled)

Claim 131 (Previously Presented): A method as defined in claim 191, wherein the biologically active agent is an interferon.

Claim 132 (Previously Presented): A method as defined in claim 191, wherein the biologically active agent is erythropoietin.

Claim 133 (Previously Presented): A method as defined in claim 191, wherein the biologically active agent is an antigen.

Claim 134 (Previously Presented): A method as defined in claim 191, wherein the biologically active agent is a peptide.

Claim 135 (Previously Presented): A method as defined in claim 134, wherein the biologically active agent is an interferon.

Claim 136 (Previously Presented): A method as defined in claim 134, wherein the biologically active agent is erythropoietin.

Claim 137 (Previously Presented): A method as defined in claim 134, wherein the biologically active agent is an antigen.

Claim 138 (Canceled):

Claim 139 (Previously Presented): The method of claim 192, wherein the biologically active agent is human growth hormone.

Claim 140 (Previously Presented): The method of claim 192, wherein the biologically active agent is growth-hormone releasing hormone.

Claim 141 (Previously Presented): The method of claim 192, wherein the biologically active agent is insulin.

Claim 142 (Previously Presented): The method of claim 192, wherein the biologically active agent is heparin.

Claim 143 (Previously Presented): The method of claim 192, wherein the biologically active agent is low molecular weight heparin.

Claim 144 (Previously Presented): The method of claim 192, wherein the biologically active agent is calcitonin.

Claim 145 (Previously Presented): The method of claim 192, wherein the biologically active agent is cromolyn sodium.

Claim 146 (Previously Presented): The method of claim 192, wherein the biologically active agent is an antimicrobial.

Claim 147 (Previously Presented): A method as defined in claim 192, wherein the biologically active agent is a peptide.

Claim 148 (Previously Presented): A method as defined in claim 147, wherein the biologically active agent is an interferon.

Claim 149 (Previously Presented): A method as defined in claim 147, wherein the biologically active agent is erythropoietin.

Claim 150 (Previously Presented): A method as defined in claim 147, wherein the biologically active agent is an antigen.

Claim 151 (Canceled):

Claim 152 (Previously Presented): The method of claim 193, wherein the biologically active agent is human growth hormone.

Claim 153 (Previously Presented): The method of claim 193, wherein the biologically active agent is growth-hormone releasing hormone.

Claim 154 (Previously Presented): The method of claim 193, wherein the biologically active agent is insulin.

Claim 155 (Previously Presented): The method of claim 193, wherein the biologically active agent is heparin.

Claim 156 (Previously Presented): The method of claim 193, wherein the biologically active agent is low molecular weight heparin.

Claim 157 (Previously Presented): The method of claim 193, wherein the biologically active agent is calcitonin.

Claim 158 (Previously Presented): The method of claim 193, wherein the biologically active agent is cromolyn sodium.

Claim 159 (Previously Presented): The method of claim 193, wherein the biologically active agent is an antimicrobial.

Claim 160 (Previously Presented): A method as defined in claim 193, wherein the biologically active agent is a peptide.

Claim 161 (Previously Presented): A method as defined in claim 160, wherein the biologically active agent is an interferon.

Claim 162 (Previously Presented): A method as defined in claim 160, wherein the biologically active agent is erythropoietin.

Claim 163 (Previously Presented): A method as defined in claim 160, wherein the biologically active agent is an antigen.

Claim 164 (Canceled):

Claim 165 (Previously Presented): The method of claim 194, wherein the biologically active agent is human growth hormone.

Claim 166 (Previously Presented): The method of claim 194, wherein the biologically active agent is growth-hormone releasing hormone.

Claim 167 (Previously Presented): The method of claim 194, wherein the biologically active agent is insulin.

Claim 168 (Previously Presented): The method of claim 194, wherein the biologically active agent is heparin.

Claim 169 (Previously Presented): The method of claim 194, wherein the biologically active agent is low molecular weight heparin.

Claim 170 (Previously Presented): The method of claim 194, wherein the biologically active agent is calcitonin.

Claim 171 (Previously Presented): The method of claim 194, wherein the biologically active agent is cromolyn sodium.

Claim 172 (Previously Presented): The method of claim 194, wherein the biologically active agent is an antimicrobial.

Claim 173 (Previously Presented): A method as defined in claim 194, wherein the biologically active agent is a peptide.

Claim 174 (Previously Presented): A method as defined in claim 173, wherein the biologically active agent is an interferon.

Claim 175 (Previously Presented): A method as defined in claim 173, wherein the biologically active agent is erythropoietin.

Claim 176 (Previously Presented): A method as defined in claim 173, wherein the biologically active agent is an antigen.

Claim 177 (Canceled):

Claim 178 (Previously Presented): The method of claim 195, wherein the biologically active agent is human growth hormone.

Claim 179 (Previously Presented): The method of claim 195, wherein the biologically active agent is growth-hormone releasing hormone.

Claim 180 (Previously Presented): The method of claim 195, wherein the biologically active agent is insulin.

Claim 181 (Previously Presented): The method of claim 195, wherein the biologically active agent is heparin.

Claim 182 (Previously Presented): The method of claim 195, wherein the biologically active agent is low molecular weight heparin.

Claim 183 (Previously Presented): The method of claim 195, wherein the biologically active agent is calcitonin.

Claim 184 (Previously Presented): The method of claim 195, wherein the biologically active agent is cromolyn sodium.

Claim 185 (Previously Presented): The method of claim 195, wherein the biologically active agent is an antimicrobial.

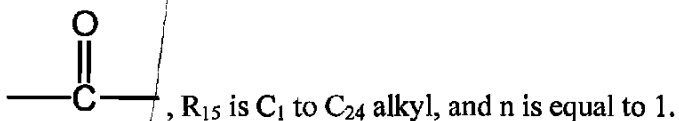
Claim 186 (Previously Presented): A method as defined in claim 195, wherein the biologically active agent is a peptide.

Claim 187 (Previously Presented): A method as defined in claim 186, wherein the biologically active agent is an interferon.

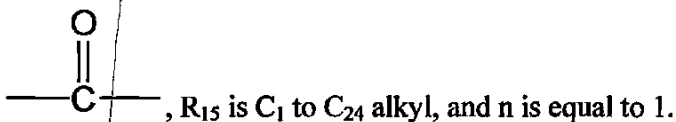
Claim 188 (Previously Presented): A method as defined in claim 186, wherein the biologically active agent is erythropoietin.

Claim 189 (Previously Presented): A method as defined in claim 186, wherein the biologically active agent is an antigen.

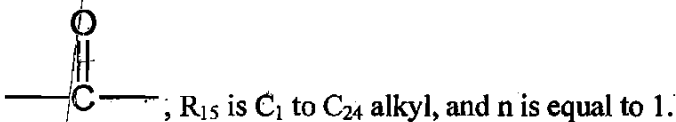
Claim 190 (Previously Presented): A method as defined in claim 13, wherein said perturbant comprises an acylated amino acid in which Ar is substituted or unsubstituted phenyl, Y is



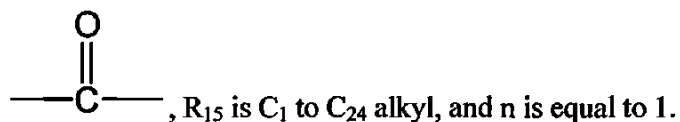
Claim 191 (Previously Presented): A method as defined in claim 23, wherein said perturbant comprises an acylated amino acid in which Ar is substituted or unsubstituted phenyl, Y is



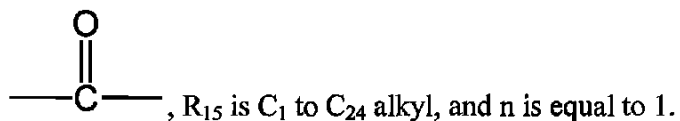
Claim 192 (Previously Presented): A method as defined in claim 50, wherein said perturbant comprises an acylated amino acid in which Ar is substituted or unsubstituted phenyl, Y is



Claim 193 (Previously Presented): A method as defined in claim 60, wherein said perturbant comprises an acylated amino acid in which Ar is substituted or unsubstituted phenyl, Y is



Claim 194 (Previously Presented): A method as defined in claim 87, wherein said perturbant comprises an acylated amino acid in which Ar is substituted or unsubstituted phenyl, Y is



Claim 195 (Previously Presented): A method as defined in claim 97, wherein said perturbant comprises an acylated amino acid in which Ar is substituted or unsubstituted phenyl, Y is

